REMARKS

This amendment is responsive to the Office Action dated July 31, 2008. Previously, Claims 1, 3, 6, 8-11, 17, 50 and 52-67 were pending and under consideration. Claims 1, 50 and 57 have been amended. Thus, Claims 1, 3, 6, 8-11, 17, 50 and 52-67 are pending and under examination.

Specific support for the amendments to Claims 1, 50 and 57 is found in the originally filed specification at page 127, Table 7.

As the amendments to the claims are fully supported by the application as filed, they present no new matter. Accordingly, entry of the present amendment to the claims is hereby respectfully requested under 37 C.F.R. §1.111.

I. Priority

The Office alleges that the disclosure of the prior-filed Application No. 60/475,402 (the '402 application) and Application No. 10/684,440 (the '440 application) fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. §112 for one or more claims in the instant application. The Office asserts that the instant application is entitled to benefit of priority to only International Patent Application No. PCT/US04/14540 (the '540 application), having a filing date of June 2, 2004. Without acquiescing to the Office's conclusion, Applicants respectfully submit that the present application is entitled at least to the priority date of the '540 application.

II. Rejection of Claims 1, 3, 17, 54 and 55 under 35 U.S.C. §102(b)

Claims 1, 3, 17, 54 and 55 stand rejected under 35 U.S.C §102(b) as allegedly being anticipated by Scanu *et al.* (International Patent Publication No. WO 1997/17371). In particular, the PTO contends that Scanu *et al.* teach a primer that is an oligonucleotide in the antisense direction and is single stranded. The antisense oligonucleotide of Scanu *et al.* is 22 nucleobases in length and is 100% complementary to nucleotides 12830-12851 of SEQ ID NO: 4.

Applicants respectfully submit that the rejection is moot in view of the amendments to the claims. As amended, Claim 1 is directed to an antisense compound 15 to 30 nucleobases in length targeted to a nucleic acid molecule encoding apolipoprotein(a), wherein said compound is at least 94% complementary to nucleotides 12380-12438 as set forth in SEQ ID NO: 4. The primers disclosed by Scanu *et al.* do not overlap the region claimed in amended Claim 1. Thus, Scanu *et al.* cannot anticipate amended Claim 1 since it fails to teach every

element of the invention as presently claimed (see MPEP 2131). Claims 3, 17, 54 and 55 are dependent upon Claim 1 and encompass every limitation of Claim 1, thus Scanu *et al.* cannot anticipate Claims 3, 17, 54 and 55.

Accordingly, Applicants assert that the rejection of Claims 1, 3, 17, 54 and 55 as anticipated by Scanu *et al.* is moot in view of the amendments to the claims and therefore respectfully request its reconsideration and withdrawal.

III. Rejection of Claims 1, 3, 6, 8-11, 17 and 54-67 under 35 U.S.C. §102(b)

Claims 1, 3, 6, 8-11, 17 and 54-67 stand rejected under 35 U.S.C §102(b) as allegedly being anticipated by Crooke *et al.* (International Patent Publication No. WO 2003/014307).

In particular, the PTO contends that Crooke *et al.* teach antisense oligonucleotides 20 nucleotides in length that are 100% complementary to nucleotides 12461-12480, nucleotides 12699-12718 and nucleotides 13354-13373.

Applicants respectfully submit that the rejection is moot in view of the amendments to the claims. As amended, Claims 1 and 57 are directed to antisense compounds 15 to 30 nucleobases in length targeted to a nucleic acid molecule encoding apolipoprotein(a), wherein said compounds are at least 94% or 90%, respectively, complementary to nucleotides 12380-12438 as set forth in SEQ ID NO: 4. The regions disclosed by Crooke *et al.* do not overlap the region claimed in amended Claims 1 and 57. Thus, Crooke *et al.* cannot anticipate amended Claims 1 and 57 since it fails to teach every element of the invention as presently claimed (see MPEP 2131). Claims 3, 6, 8-11, 17, 54-56 and 58-67 are dependent upon Claims 1 or 57 and encompass every limitation of Claims 1 or 57, thus Crooke *et al.* cannot anticipate Claims 1, 3, 6, 8-11, 17 and 54-67.

Accordingly, Applicants assert that the rejection of Claims 1, 3, 6, 8-11, 17 and 54-67 as anticipated by Crooke *et al.* is moot in view of the amendments to the claims and therefore respectfully request its reconsideration and withdrawal.

IV. Rejection of Claims 1, 3, 6, 8-11, 17 and 52-67 under 35 U.S.C. §103(a)

Claims 1, 3, 6, 8-11, 17, 52-67 are rejected under 35 U.S.C §103(a) as allegedly obvious. Applicants respectfully submit that the references cited by the Office, whether considered alone or in combination, fail to teach or suggest each and every element of the invention recited by the pending claims of the present application. Thus, Applicants respectfully submit that the claims are not obvious over the combination of references cited by the Office, as discussed in detail below.

A. The Cited References Do Not Teach or Suggest All Claim Limitations of Claims 1, 3, 6, 8-11, 17, 54-67

Claims 1, 3, 6, 8-11, 17, 54-67 were rejected under 35 U.S.C §103(a) as allegedly unpatentable over Ruoy *et al.* (International Patent Publication No. WO 99/65241) in view of Stinchcomb *et al.* (International Patent Publication No. WO 96/09392), Olie *el al.* (Biochimia et Biophysica Acta, 2002, 1576:101-109), Baracchini *et al.* (U.S. Patent No. 5,801,154) and Ramaswamy et al (U.S. Patent No. 6,525,191).

Applicants respectfully disagree, however in order to advance prosecution, the claims have been amended to recite oligonucleotides complementary to region 12380-12438 of apolipoprotein(a). The claims as amended are not directed to regions specifically targeted by Stinchcomb *et al.* and, as described in detail below, none of the cited references provide a reason why nucleotides 12380-12438 as claimed, out of the entire coding sequence of apolipoprotein(a), should be targeted.

Ruoy *et al.* neither teach nor suggest that an antisense compound should be targeted to any particular region of the coding region of apolipoprotein(a) much less the region claimed. As the Office acknowledges, Ruoy *et al.* do not teach antisense compounds that are at least 90% complementary to nucleotides 12380-13493 of apolipoprotein (a) SEQ ID: 4 or the specific modifications that are instantly claimed (Office Action page 8, 2nd paragraph).

Stinchcomb *et al.* do not teach that sequence 12380-12438 as claimed should be targeted. Therefore, Stinchcomb *et al.* cannot remedy the deficiency of Ruoy *et al.*

Olie *et al.* do not teach any antisense compounds directed to apolipoprotein (a), much less the specific region specified in the claims. Therefore, Olie *et al.* cannot remedy the deficiencies of Ruoy *et al.* and Stinchcomb *et al.*

Baracchini *et al.* do not teach or suggest anything regarding antisense modulation of apolipoprotein(a) expression. Baracchini *et al.* do not teach or suggest that nucleotides 12380-12438 of SEQ ID NO: 4 should be targeted. As such, Baracchini *et al.* cannot cure the deficiencies of Ruoy *et al.*, Stinchcomb *et al.* and Olie *et al.* discussed above.

Ramaswamy *et al.* do not teach or suggest anything regarding antisense modulation of apolipoprotein(a) expression. Ramaswamy *et al.* do not teach or suggest that nucleotides 12380-12438 of SEQ ID NO: 4 should be targeted. As such, Ramaswamy *et al.* cannot cure the deficiencies of Ruoy *et al.*, Stinchcomb *et al.*, Olie *et al.* and Baracchini *et al.* discussed above.

The combination of references, when considered as a whole, fails to teach or suggest each and every element of the invention as presently claimed. In particular, the Office contends that it would have been obvious to a person of ordinary skill in the art to make an antisense oligonucleotide as taught by Ruoy *et al.*, and targeted to the specific target regions of Stinchcomb *et al.* and that one skilled in the art would have been motivated to target the specific coding region of apolipoprotein (a), as taught by Stinchcomb *et al.* (Office Action page 10, 3rd-4th paragraphs). Applicants respectfully disagree, however in order to advance prosecution, the claims have been amended to recite oligonucleotides complementary to the region 12380-12438 of apolipoprotein(a). The claims as amended are not directed to regions specifically targeted by Stinchcomb *et al.* and none of the cited references provide a reason why nucleotides 12380-12438 as claimed, out of the entire coding sequence of apolipoprotein(a), should be targeted.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to the claims under 35 U.S.C §103(a).

B. The Cited References Do Not Teach or Suggest All Claim Limitations of Claims 1, 3, 6, 8-11, 17, 52-67

Claims 1, 3, 6, 8-11, 17, 52-67 were rejected under 35 U.S.C §103(a) as allegedly unpatentable over Elbashir *et al.* (EMBO, 2001, 20(23):6877-6888) in view of Stinchcomb *et al.* (International Patent Publication No. WO 96/09392), Tuschl *et al.* (The siRNA user guide, pages 1, 3 and 5, 8/26/01), Holen *et al.* (Nucleic acids Research, 2002, 30(8):1757-1766), Olie *el al.* (Biochimia et Biophysica Acta, 2002, 1576:101-109), Baracchini *et al.* (U.S. Patent No. 5,801,154) and Ramaswamy et al (U.S. Patent No. 6,525,191).

Applicants respectfully disagree, however in order to advance prosecution, the claims have been amended to recite oligonucleotides complementary to the region 12380-12438 of apolipoprotein(a). The claims as amended are not directed to regions specifically targeted by Stinchcomb *et al.* and none of the cited references provide a reason why nucleotides 12380-12438 as claimed, out of the entire coding sequence of apolipoprotein(a), should be targeted.

Elbashir *et al.*, as the Office acknowledges, do not teach targeting apolipoprotein(a) (Office Action page 14, 2nd paragraph). Thus, Elbashir *et al.* do not teach the claimed invention i.e., an antisense compound 15 to 30 nucleobases long with at least 94% complementarity to targeted nucleotides 12380-12438 of apolipoprotein (a).

Stinchcomb *et al.* do not teach that sequence 12380-12438 as claimed should be targeted. Therefore, Stinchcomb *et al.* cannot remedy the deficiency of Elbashir *et al.*

Tuschl *et al.* do not teach that sequence 12380-12438 out of the nearly 14,000 nucleotides encoding apolipoprotein (a) should be targeted as claimed. Therefore, Tuschl *et al.* cannot remedy the deficiencies of Elbashir *et al.* and Stinchcomb *et al.*

Holen *et al.* do not teach targeting apolipoprotein(a) much less sequence 12380-12438 as claimed. Therefore, Holen *et al.* cannot remedy the deficiencies of Elbashir *et al.*, Stinchcomb *et al.* and Tuschl *et al.*

Olie *et al.*, Baracchini *et al.* and Ramaswamy *et al.* were discussed *supra.* None of these references teaches targeting apolipoprotein(a) much less sequence 12380-12438 as claimed. Therefore, the combination of Olie *et al.*, Baracchini *et al.* and Ramaswamy *et al.* cannot remedy the deficiencies of Elbashir *et al.*, Stinchcomb *et al.*, Tuschl *et al.* and Holen *et al.*

The Office contends that it would have been obvious to design a siRNA as taught by Elbashir *et al.* targeted to the claimed nucleotides with the claimed stringency requirements (Office Action, page 17, 3rd paragraph). Additionally, the Office alleges that it is obvious to perform routine optimization to walk the known target sequence to design any given siRNA against the sequence in view of the guidelines taught by Elbashir *et al.*, Tuschl *et al.* and Holen *et al.*, (page 17, 4th paragraph); that as evidenced by Stinchcomb *et al.*, one would have been motivated to inhibit the expression of apolipoprotein(a) (page 18, 2nd paragraph); and that one would have been motivated to incorporate the modifications of Olie *et al.*, Baracchini *et al.* and Ramaswamy *et al.* into the siRNA of Elbashir (page 20, 1st paragraph).

Applicants respectfully disagree. None of the references cited by the Office specifically teach oligonucleotides complementary to the claimed region 12380-12438 of apolipoprotein(a). Applicants respectfully point out that the claims as amended are not directed to regions specifically targeted by Stinchcomb *et al.* and the references cited provide no reason why nucleotides 12380-12438 as claimed, out of the entire coding sequence of apolipoprotein(a), should be targeted. Thus, the combination of references fails to teach or suggest each and every element of the invention as presently claimed.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to the claims under 35 U.S.C §103(a).

CONCLUSION

In light of the above remarks, Applicants respectfully request that the Office reconsider this application with a view towards allowance. If any issues require clarification, the Office is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

No fees except the fee for a two month time extension are due for this Amendment. However, should any additional fees be deemed necessary, the Commissioner is herby authorized to charge such fees to Deposit Account 50-0252 referencing case number ISPH-0595USA.

Respectfully submitted,

Date: 12/23/08

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